

SEQUENCE LISTING

<110> Ono et al.
 <120> Modified antibodies recognizing receptor trimers or higher multimers
 <130> 75996-01
 <150> PCT/JP2004/018507
 <151> 2004-12-10
 <150> JP 2003-415735
 <151> 2003-12-12
 <160> 42
 <170> PatentIn version 3.1
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 <212> DNA
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 <223> An artificially synthesized nucleotide sequence

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 ctgagactct cctgtgcagc ctctggattc accttttagca gctatgccat gagctgggtc 180
 cgccaggctc caggggaagg gctggagtgg gtctcagcta ttagtggttag tggtagtagc 240
 agatactacg cagactccgt gaagggccgg ttcaccatct ccagagacaa ttccaagaac 300
 acgctgtatc tgcaaatgaa cagcctgaga gccgaggaca cggccgtata ttactgtgctg 360
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 gtctcctcag gtggagaaat tgtgctgact cagtctccag actttcagtc tgtgactcca 480
 aaggagaaaag tcaccatcac ctgccgggcc agtcagagca ttggtagtag cttacactgg 540
 taccagcaga aaccagatca gtctccaaag ctctcatca agtatgcttc ccagtccttc 600
 tcaggggtcc cctcgagggt cagtggcagt ggatctggga cagatttcac cctcaccatc 660
 aatagcctgg aagctgaaga tgctgcagcg tattactgtc atcagagtag tagtttaccg 720
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<213> Artificial

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Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly
1 5 10 15

Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Glu Ile Val
130 135 140

Leu Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val
145 150 155 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp
165 170 175

Tyr Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala
180 185 190

Ser Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
195 200 205

Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala
210 215 220

Ala Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Ile Thr Phe Gly
225 230 235 240

Gln Gly Thr Arg Leu Glu Ile Lys Asp Tyr Lys Asp Asp Asp Asp Lys
245 250 255

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 gtctcctcag gtgaaattgt gctgactcag tctccagact ttcagtctgt gactccaaag 480
 gagaaagtca ccatcacctg ccggggccagt cagagcattg gtagtagctt aactgggtac 540
 cagcagaaac cagatcagtc tccaaagctc ctcatcaagt atgcttccca gtccttctca 600
 ggggtcccct cgagggttcag tggcagtgga tctgggacag atttcaccct caccatcaat 660
 agcctggaag ctgaagatgc tgcagcgtat tactgtcatc agagtagtag tttaccgatc 720
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 Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
 20 25 30
 Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
 35 40 45
 Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu

50	55	60
Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala		
65	70	75 80
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn		
	85	90 95
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val		
	100	105 110
Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr		
	115	120 125
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Glu Ile Val Leu		
	130	135 140
Thr Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val Thr		
	145	150 155 160
Ile Thr Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser Leu His Trp Tyr		
	165	170 175
Gln Gln Lys Pro Asp Gln Ser Pro Lys Leu Leu Ile Lys Tyr Ala Ser		
	180	185 190
Gln Ser Phe Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly		
	195	200 205
Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala		
	210	215 220
Ala Tyr Tyr Cys His Gln Ser Ser Ser Leu Pro Ile Thr Phe Gly Gln		
	225	230 235 240
Gly Thr Arg Leu Glu Ile Lys Asp Tyr Lys Asp Asp Asp Asp Lys		
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<213> Artificial

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ctgagactct cctgtgcagc ctctggattc accttagca gctatgcat gagctgggtc	180
cgccaggctc caggggaagg gctggagtgg gtctcagcta ttagtggttag tggtagtagc	240
agatactacg cagactccgt gaagggccgg ttcaccatct ccagagacaa ttccaagaac	300

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acgctgtatc tgcaaatgaa cagcctgaga gccgaggaca cggccgtata ttactgtgcg      360
aaagagagca gtggctggtt cggggccttt gactactggg gccagggaac cctggtcacc      420
gtctcctcag aaattgtgct gactcagtct ccagactttc agtctgtgac tccaaaggag      480
aaagtcacca tcacctgccg ggccagtcag agcattggta gtagcttaca ctggtaccag      540
cagaaaccag atcagtctcc aaagctcctc atcaagtatg cttcccagtc cttctcaggg      600
gtcccctcga ggttcagtgg cagtggatct gggacagatt tcaccctcac catcaatagc      660
ctggaagctg aagatgctgc agcgtattac tgtcatcaga gtagtagttt accgatcacc      720
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<210> 6
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<213> Artificial

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<223> An artificially synthesized peptide sequence

<400> 6

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Met Glu Phe Gly Leu Ser Trp Leu Phe Leu Val Ala Ile Leu Lys Gly
1           5           10          15

Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
20          25          30

Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35          40          45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50          55          60

Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala
65          70          75          80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85          90          95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100         105         110

Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr
115         120         125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Glu Ile Val Leu Thr
130         135         140

Gln Ser Pro Asp Phe Gln Ser Val Thr Pro Lys Glu Lys Val Thr Ile

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145		150		155		160									
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				165					170					175	
Gln	Lys	Pro	Asp	Gln	Ser	Pro	Lys	Leu	Leu	Ile	Lys	Tyr	Ala	Ser	Gln
			180					185					190		
Ser	Phe	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr
		195					200					205			
Asp	Phe	Thr	Leu	Thr	Ile	Asn	Ser	Leu	Glu	Ala	Glu	Asp	Ala	Ala	Ala
	210					215					220				
Tyr	Tyr	Cys	His	Gln	Ser	Ser	Ser	Leu	Pro	Ile	Thr	Phe	Gly	Gln	Gly
225					230					235					240
Thr	Arg	Leu	Glu	Ile	Lys	Asp	Tyr	Lys	Asp	Asp	Asp	Asp	Lys		
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 <211> 1538
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 ctgagactct cctgtgcagc ctctggattc accttagca gctatgccat gagctgggtc 180
 cgccaggctc caggggaagg gctggagtgg gtctcagcta ttagtggtag tggtggtagc 240
 agatactacg cagactccgt gaagggccgg ttcaccatct ccagagacaa ttccaagaac 300
 acgctgtatc tgcaaatgaa cagcctgaga gccgaggaca cggccgtata ttactgtgcg 360
 aaagagagca gtggctgggt cggggccttt gactactggg gccagggaac cctggtcacc 420
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 ctcaccatca atagcctgga agctgaagat gctgcagcgt attactgtca tcagagtagt 720
 agtttaccga tcaccttcgg ccaagggaca cgactggaga ttaaagagc tgatgctgca 780
 gctgcaggag gtccccgggtc cgagggtacag ctgttgaggt ctgggggagg cttggtacag 840

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agtggtggtg gcagatacta cgcagactcc gtgaagggcc gggtcaccat ctccagagac     1020
aattccaaga acacgctgta tctgcaaatg aacagcctga gagccgagga cacggccgta     1080
tattactgtg cgaaagagag cagtggctgg ttcggggcct ttgactactg gggccagggg     1140
accctgggtc ccgtctcctc aggtggaggc ggatcggaaa ttgtgctgac tcagtctcca     1200
gactttcagt ctgtgactcc aaaggagaaa gtcaccatca cctgccgggc cagtcagagc     1260
attggtagta gcttacactg gtaccagcag aaaccagatc agtctccaaa gctcctcatc     1320
aagtatgctt cccagtcctt ctcaggggtc ccctcgaggt tcagtggcag tggatctggg     1380
acagatttca ccctcaccat caatagcctg gaagctgaag atgctgcagc gtattactgt     1440
catcagagta gtagtttacc gatcaccttc ggccaagggg cacgactgga gattaaagac     1500
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<212> PRT

<213> Artificial

<220>

<223> An artificially synthesized peptide sequence

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Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln
          20           25           30

```

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Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
          35           40           45

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Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
          50           55           60

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Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Arg Tyr Tyr Ala
65           70           75           80

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Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
          85           90           95

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Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
          100          105          110

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Tyr Tyr Cys Ala Lys Glu Ser Ser Gly Trp Phe Gly Ala Phe Asp Tyr

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115					120					125				
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Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Asp	Phe	Gln	Ser	Val	Thr	Pro
145					150					155				160
Glu	Lys	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln	Ser	Ile	Gly	Ser
				165					170					175
Leu	His	Trp	Tyr	Gln	Gln	Lys	Pro	Asp	Gln	Ser	Pro	Lys	Leu	Leu
			180					185					190	Ile
Lys	Tyr	Ala	Ser	Gln	Ser	Phe	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser
		195					200					205		Gly
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asn	Ser	Leu	Glu
						215					220			Ala
Glu	Asp	Ala	Ala	Ala	Tyr	Tyr	Cys	His	Gln	Ser	Ser	Ser	Leu	Pro
225						230					235			240
Thr	Phe	Gly	Gln	Gly	Thr	Arg	Leu	Glu	Ile	Lys	Arg	Ala	Asp	Ala
				245					250					255
Ala	Ala	Gly	Gly	Pro	Gly	Ser	Glu	Val	Gln	Leu	Leu	Glu	Ser	Gly
				260				265						270
Gly	Leu	Val	Gln	Pro	Gly	Arg	Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala
		275					280					285		Ser
Gly	Phe	Thr	Phe	Ser	Ser	Tyr	Ala	Met	Ser	Trp	Val	Arg	Gln	Ala
						295					300			Pro
Gly	Lys	Gly	Leu	Glu	Trp	Val	Ser	Ala	Ile	Ser	Gly	Ser	Gly	Ser
305						310					315			320
Arg	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg
				325					330					335
Asn	Ser	Lys	Asn	Thr	Leu	Tyr	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala
			340					345					350	Glu
Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Lys	Glu	Ser	Ser	Gly	Trp	Phe
		355					360					365		Gly
Ala	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser
		370					375					380		Gly
Gly	Gly	Gly	Ser	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Asp	Phe	Gln
385						390					395			400
Val	Thr	Pro	Lys	Glu	Lys	Val	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Gln
				405					410					415
Ile	Gly	Ser	Ser	Leu	His	Trp	Tyr	Gln	Gln	Lys	Pro	Asp	Gln	Ser
														Pro

420	425	430
Lys Leu Leu Ile Lys Tyr Ala Ser Gln Ser Phe Ser Gly Val Pro Ser		
435	440	445
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn		
450	455	460
Ser Leu Glu Ala Glu Asp Ala Ala Ala Tyr Tyr Cys His Gln Ser Ser		
465	470	475
Ser Leu Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Asp		
485	490	495
Tyr Lys Asp Asp Asp Asp Lys		
500		

<210> 9
 <211> 15
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 <213> Artificial

<220>
 <223> An artificial sequence encoding linker sequence

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15

<210> 10
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 <212> PRT
 <213> Artificial

<220>
 <223> An artificially synthesized linker sequence

<400> 10
 Gly Gly Gly Gly Ser
 1 5

<210> 11
 <211> 24
 <212> DNA
 <213> Artificial

<220>
 <223> An artificial sequence encoding flag tag sequence

<400> 11
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24

<210> 12
 <211> 8

<212> PRT
<213> Artificial

<220>

<223> An artificially synthesized flag tag sequence

<400> 12

Asp Tyr Lys Asp Asp Asp Asp Lys
1 5

<210> 13

<211> 806

<212> DNA

<213> Artificial

<220>

<223> An artificially synthesized diabody sequence

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ctgagactct cctgtgcagc ctctggattc accttttagca gctatgccat gagctgggtc	180
cgccaggctc caggggaagg gctggagtgg gtctcagcta ttagtggtag tggtagtagc	240
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gtctcctcag gtggaggcgg atcggaatt gtgctgactc agtctccaga ctttcagtct	480
gtgactccaa aggagaaaagt caccatcacc tgccgggcca gtcagagcat tggtagtagc	540
ttacactggg accagcagaa accagatcag tctccaaaagc tcctcatcaa gtatgcttcc	600
cagtccttct caggggtccc ctcgagggtc agtggcagtg gatctgggac agatttcacc	660
ctcaccatca atagcctgga agctgaagat gctgcagcgt attactgtca tcagagtagt	720
agtttaccga tcaccttcgg ccaagggaca cgactggaga ttaaagacta caaggatgac	780
gacgataagt gataagcggc cgcaat	806

<210> 14

<211> 94

<212> DNA

<213> Artificial

<220>

<223> An artificially synthesized oligonucleotide sequence

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gtccagtgtg aggtacagct gttggagtct gggg 94

<210> 15
<211> 96
<212> DNA
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<220>
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<400> 15
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agcctccccc agactccaac agctgtacct cacact 96

<210> 16
<211> 97
<212> DNA
<213> Artificial

<220>
<223> An artificially synthesized oligonucleotide sequence

<400> 16
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caggggaaggg gctggagtgg gtctcagcta ttagtgg 97

<210> 17
<211> 99
<212> DNA
<213> Artificial

<220>
<223> An artificially synthesized oligonucleotide sequence

<400> 17
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ccaccactac cactaatagc tgagaccacac tccagcccc 99

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<211> 103
<212> DNA
<213> Artificial

<220>
<223> An artificially synthesized oligonucleotide sequence

<400> 18

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gagagccgag gacacggccg tatattactg tgcgaaagag agc 103

<210> 19
<211> 87
<212> DNA
<213> Artificial

<220>
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<400> 19
ggagacggtg accagggttc cctggcccca gtagtcaaag gccccgaacc agccactgct 60
ctctttcgca cagtaatata cggccgt 87

<210> 20
<211> 98
<212> DNA
<213> Artificial

<220>
<223> An artificially synthesized oligonucleotide sequence

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actcagtctc cagactttca gtctgtgact ccaaagga 98

<210> 21
<211> 79
<212> DNA
<213> Artificial

<220>
<223> An artificially synthesized oligonucleotide sequence

<400> 21
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cacagactga aagtctgga 79

<210> 22
<211> 103
<212> DNA
<213> Artificial

<220>
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<400> 22
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ccaaagctcc tcatcaagta tgcttcccag tccttctcag ggg 103

<210> 23

<211> 97

<212> DNA

<213> Artificial

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<223> An artificially synthesized oligonucleotide sequence

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gaggggaccc ctgagaagga ctgggaagca tacttga 97

<210> 24

<211> 90

<212> DNA

<213> Artificial

<220>

<223> An artificially synthesized oligonucleotide sequence

<400> 24

tttcaccctc accatcaata gcctggaagc tgaagatgct gcagcgtatt actgtcatca 60

gagtagtagt ttaccgatca ccttcggcca 90

<210> 25

<211> 93

<212> DNA

<213> Artificial

<220>

<223> An artificially synthesized oligonucleotide sequence

<400> 25

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ccttggccga aggtgatcgg taaactacta ctc 93

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<211> 26

<212> DNA

<213> Artificial

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<223> An artificially synthesized primer sequence

<400> 26

tagaattcca ccatggagtt tgggct 26

<210> 27
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 <212> DNA
 <213> Artificial

 <220>
 <223> An artificially synthesized primer sequence

 <400> 27
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<210> 28
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 <212> DNA
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<210> 29
 <211> 26
 <212> DNA
 <213> Artificial

 <220>
 <223> An artificially synthesized primer sequence

 <400> 29
 attgcggccg cttatcactt atcgtc 26

<210> 30
 <211> 35
 <212> DNA
 <213> Artificial

 <220>
 <223> An artificially synthesized primer sequence

 <400> 30
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<210> 31
 <211> 36
 <212> DNA
 <213> Artificial

 <220>
 <223> An artificially synthesized primer sequence

<400> 31
 aatttctcca cctgaggaga cggtgaccag gggtcc 36

<210> 32
 <211> 32
 <212> DNA
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 <212> DNA
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<210> 35
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